tetramer and both monomeric peptides (RTR and RTRGG) were tested, separately, for inhibition of the ultrafiltered tripeptide chemoattractants or LTB_4.

The complementary RTR tetrameric peptide was a powerful antagonist of N-acetyl-PGP induced polymorphonuclear leukocyte polarization (ID_{50} of 200 nM). The RTR dimer was much less potent (ID_{50} of 105 μM). Both monomeric peptides, RTR and RTRGG, were only antagonistic at millimolar concentrations. The ASA tetramer showed no capacity to inhibit N-acetyl-PGP. The RTR tetramer also inhibited polymorphonuclear leukocyte activation by the ultrafiltered tripeptide chemoattractants (ID_{50} of 30 μM), but had no effect on LTB_4. A complementary peptide (RTR) was designed which is an effective inhibitor of the neutrophil chemoattractant, N-acetyl-PGP. The peptide's potency is dramatically enhanced by tetramerization. Inhibition of this chemoattractant in the alkali-injured eye by complementary peptides offers great promise for control of the inflammatory response attendant to such injuries.

In one embodiment, the present invention is directed to a pharmaceutical composition for ophthalmologic uses. Specifically, this composition is a complementary peptide which comprises complementary sequences to proline-glycine-proline (PGP). Generally, the complementary sequences are designed based on the possible coding triplet for proline and glycine and on the hydropathic value of the two amino acids. Enhancement of the potency of the complementary sequence was achieved with a multimerization process. The resulting molecule can be divided into 4 specific subunits, connected by amide bonds with different functions: 1) recognition subunit 2) core multimerizing subunit 3) spacer subunit and 4) R N-terminal subunit.

Recognition subunit: the complementary sequence to Pro-Gly-Pro, this subunit is responsible for the interaction with the chemoattractant. It is present as a single unit in the monomer, is repeated twice in the dimer, 4 times in the tetramer and 8 times in the octamer. The recognition subunit is defined by the sequence all-L Arg-Thr-Arg and by the sequence all-L Xxx-Thr-Arg (Xxx = the 20 natural amino acids), and by all-D Arg-Thr-Arg and all-D Xxx-Thr-Arg (Xxx = the 20 natural amino acids).

The core multimerizing subunit, absent from the linear monomers, is characterized by a branching di-amino amino acid (lysine, di-amino propionic acid, di-amino butyric acid) connected to a single alanine, where both amino groups are involved in an amide bond. The function of the core is to determine the number of recognition units in the molecule and to control the relative spatial distribution of the recognition subunits. The core also represents the connection point to the resin during Solid Phase Peptide Synthesis. The octameric core is defined by the formula all-L $(((B)_2B)_2)$B-Ala, the tetramer by all-L $(B)_2$B-Ala and the dimer by all-L B-Ala (where B= lysine, di-amino propionic acid and di-amino butyric acid). The core was also obtained with all-D amino acids with the same generic formulas.

The spacers represent the connection point between the core and the recognition subunits and determines the relative spatial distribution of the recognition subunits. It can be constituted by a di-glycine. The di-glycine could be substituted by a single amino acid with the formula: $NH_2[CH_2]_n$-COOH [n=2[3-amino propionic acid];3;4;5;6;or 7[8-amino caprylic acid]].